PATENT
Docket No.: **19603/3357 (CRF D-1585G)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Barany et al.	Examiner: To Be Assigned
Serial No.	:	09/986,527	
Cnfrm. No.	:	5780	Art Unit: 1627
Filed	:	November 9, 2001	
For	:	DETECTION OF NUCLEIC ACID SEQUENCE DIFFERENCES USING THE LIGASE DETECTION REACTION WITH ADDRESSABLE ARRAYS	

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Transmitted herewith in the above-identified application are:

[X] Request for Declaration of Interference Under 37 CFR § 1.607(a) (17 pages);

[X] Showing by Applicant Under 37 CFR § 1.608(b) (64 pages);

[X] Declaration of Francis Barany Under 37 CFR § 1.608(b) (15 pages) with Appendices 1-3;

[X] Declaration of Donald Bergstrom Under 37 CFR § 1.608(b) (4 pages) with Appendices 1-3;

[X] Declaration of Gregory W. Siskind Under 37 CFR § 1.608(b) (2 pages) with Appendix 1;

[X] Declaration of Gerald Zon Under 37 CFR § 1.608(b) (2 pages) with Appendices 1-3; and

[X] A self-addressed, prepaid postcard for acknowledging receipt.

[X] The Commissioner is hereby authorized to charge any necessary fees to Deposit Account No. **14-1138**.

A duplicate copy of this sheet is enclosed.

Date: January 7, 2002

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Jan. 7, 2002 — Date

Ruth R. Smith — Ruth R. Smith

PATENT
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SHOWING BY APPLICANT UNDER 37 CFR § 1.608(b)

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 CFR § 1.608(b), applicants hereby submit this paper in support of their accompanying Request for Declaration of Interference Under 37 CFR § 1.607(a) between the above-identified application and U.S. Patent No. 6,156,501 to McGall et al. ("'501 patent"). As demonstrated *infra*, an interference should be declared, because: (1) applicants first conceived of the claimed subject matter of the present application which was then derived from them by the inventors of the '501 patent, and (2) the subject matter of the '501 patent is not patentable to the inventors of the '501 patent.

I. Background

A. Present Application's History

The present application was filed on November 9, 2001, pursuant to 37 CFR § 1.53(b), as a continuation-in-part of U.S. Patent Application Serial No. 08/794,851 ("parent

application") which was filed on February 4, 1997, now pending. The parent application claims priority, under 35 U.S.C. § 119, to U.S. Provisional Patent Application Serial No. 60/011,359, filed February 9, 1996 ("grandparent application"). A sentence stating this has been inserted at the beginning of the present application. The present application identifies Francis Barany, George Barany, and Robert P. Hammer ("Barany et al.") as inventors. The present continuation-in-part application uses virtually the same disclosure as the parent application and the grandparent application, both of which support all pending claims, pursuant to 35 U.S.C. § 112 (first paragraph), as described *infra*.

B. Present Application's Subject Matter

As set forth in the attached Declaration of Francis Barany Under 37 CFR § 1.608(b) ("Barany Declaration"), the present application relates to a method of detecting nucleic acid sequence differences in target nucleic acids by the use of a solid support with an array of DNA oligonucleotides or peptide nucleotide analogue ("PNA") oligomers to capture and detect the products of ligase detection reaction ("LDR") (see page 1, lines 13-22, page 8, lines 10-13, page 30, lines 32-34, and page 40, lines 35-37 of the present application) (Barany Declaration ¶ 19). The present application further teaches (at page 16, line 23 to page 19, line 5 and in the drawings that these pages describe) that each ligation product of the LDR process is provided with an addressable array specific portion which is selectively captured by a complementary capture probe at a particular location on the solid support (Barany Declaration ¶ 19). The present application further discloses that the array of capture probes on the solid support can be designed to achieve optimal hybridization to the addressable array specific portion of the ligation product (see page 35, lines 12-15 and page 49, lines 16-18) (Barany Declaration ¶ 19). This is achieved by increasing thermal stability through reduction of the difference in melting temperature (i.e. T_m) between the different duplexes formed by LDR products having an addressable array-specific portion and the complementary capture probe (i.e. DNA oligonucleotides or PNA oligomers) hybridized to one another on the solid support (Id. at page 35, lines 12-15) (Barany Declaration ¶ 19). These differences in melting temperature result from differences in G•C/A•T content (Id.) (Barany Declaration ¶ 19).

C. Grant Application's Subject Matter

On or before February 4, 1994, a grant application, entitled "New Methods for Cancer Detection", ("Grant Application") was submitted to the National Cancer Institute, U.S. Department of Health and Human Services ("NCI") by, amongst others, Francis Barany, Donald Bergstrom, and co-inventors George Barany and Robert Hammer (Barany Declaration ¶ 5). The Grant Application describes five (5) projects, including Project 5, entitled "Design and Synthesis of DNA and PNA Arrays" (Barany Declaration ¶ 5). A copy of relevant portions of the Grant Application, including the Project 5 description, is attached as Appendix 1 of the Barany Declaration (Barany Declaration ¶ 5).

Project 5 describes a method of detecting nucleic acid sequence differences in target nucleic acids by the use of a solid support with an array of peptide nucleotide analogues ("PNA") to capture and detect the products of a ligase detection reaction ("LDR") (Appendix 1 of Barany Declaration, p. 19-22) (Barany Declaration ¶ 6). The subject matter of the claims of the present application is described in the Grant Application as follows (see also the Barany Declaration at ¶¶ 7-16):

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (Appendix 1 of Barany Declaration, p. 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
an array of a plurality of oligonucleotide analogue probes having different sequences,	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9).
wherein said oligonucleotide analogue probes are	Discloses PNA oligomers in unique addressable

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coupled to a solid substrate at known locations and	arrays (Id. at 21, lines 27-30). Discloses a PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44).
with a similar hybridization stability across the array.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10). Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.	Discloses solid support of modified glass, plastic, or cellulose surfaces, polyethylene glycol-polystyrene beads, or membranes (Id. at 26, lines 1-2). Discloses that solid support can be beads, membranes, or surfaces (Id. at 27, lines 1-2 of description of Figure 6; Id. at 29, line 17 to 30, line 9; Figure 8). Discloses the use of glass and derivatized membrane supports (Id. at 21, lines 8-9).
4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.	Discloses assembling arrays with tetramers to produce capture oligonucleotides up to 24 nucleotides in length (Id. at 23, line 1 to 25, Table

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	1; Id. at 26, Table 2; Id. at 29, line 1 to 34, line 35).
5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a peptide nucleic acid.	Discloses complementary zip codes prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (Id. at 11, lines 7; Id. at 23, lines 20-21).
6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.	Discloses a universal PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54; Id. at 31, lines 30-31).
7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.	Discloses the preparation of DNA or PNA synthetic probes, with either all thymine or all 5-propynyl-uracil (Id. at 22, lines 20-21; Id. at 23, lines 20-21).
8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.	Discloses the use of photolabile *o*-nitrobenzyl linkers (Id. at 30, lines 6-7).
9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses treatment of the support surface with side-chain functionalized alkyltrichlorosilane (Id. at 26, lines 5-8).
10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.	Discloses process for manufacturing a PNA oligomer array by application of solution including protected PNA tetramers to the solid support using a prefabricated mask (Id. at 31, line 38 to 34, line 35).
11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses treatment of the support surface with side-chain functionalized alkyltrichlorosilane (Id. at 26, lines 5-8).
12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44). Discloses a plurality of different sequences attached at different locations (addresses) on a solid support (Id. at 19, lines 36-44). Discloses a universal PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54).
hybridized to complementary oligonucleotide analogue targets,	Discloses LDR products having a zip code tail which hybridize to complementary zip codes on a solid support where the complementary components are DNA or PNA (Id. at 21, lines 4-6).

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	Replaces thymine with 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 11, lines 8-10; Id. at 24, lines 8-9).
wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10). Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.	Discloses complementary zip codes prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (Id. at 11, line 7; Id. at 23, lines 20-21).
15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids using an array of oligonucleotides on a solid support to capture complementary zip code tails on LDR products (Id. at 11, lines 4-6).
(a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences,	Discloses DNA oligonucleotides or PNA oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses that thymine can be

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	replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations,	Discloses PNA oligomers in unique addressable arrays (Id. at 21, lines 27-30). Discloses a PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
said solid substrate having a surface;	Discloses a solid support having a surface (Id. at 21, lines 4-5, 31, and 48-49; Id. at 25, lines 9-12).
(b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses contacting ligated reaction product with a solid support including complementary zip codes (DNA oligonucleotides or PNA oligomers) which are complementary to addressable array-specific portions (zip codes) of a ligated product sequence (Id. at 11, lines 4-7). The zip code tail of the ligated reaction product will be captured by a complementary zip code on the solid support (Id. at 11, lines 5-6). Discloses incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences (Id. at 11, lines 8-10).
with a similar hybridization stability across the array; and	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
(c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (Id. at 19, line 44, to 21, line 25; Figure 2).
16. The method of claim 15, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10).

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complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.	Discloses the detection of the R248 mutation of the p53 tumor suppression gene (Id. at 19, line 44 to 21, end of description of Figure 2; Figure 2).
18. The method of claim 15, wherein said target nucleic acid is amplified prior to said hybridization step.	Discloses a polymerase chain reaction/ligase detection reaction method (Id. at 16, lines 4-7).
19. The method of claim 15, wherein said plurality of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.	Discloses the use of photolabile *o*-nitrobenzyl linkers (Id. at 30, lines 6-7).
20. The method of claim 15, wherein said plurality of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.	Discloses process for manufacturing a PNA oligomer array by application of solution including protected PNA tetramers to the solid support using a prefabricated mask (Id. at 31, line 38 to 34, line 35).
21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.	Discloses solid support of modified glass, plastic, or cellulose surfaces, polyethylene glycol-polystyrene beads, or membranes (Id. at 26, lines 1-2). Discloses that solid support can be beads, membranes, or surfaces (Id. at 27, lines 1-2 of description of Figure 6; Id. at 29, line 17 to 30, line 9; Figure 8). Discloses the use of glass and derivatized membrane supports (Id. at 21, lines 8-9).
22. The method of claim 15, wherein said solid substrate is comprised of materials selected from the group consisting of silica, polymers and glass.	Discloses solid support of modified glass, plastic, or cellulose surfaces, polyethylene glycol-polystyrene beads, or membranes (Id. at 26, lines 1-2). Discloses that solid support can be beads, membranes, or surfaces (Id. at 27, lines 1-2 of description of Figure 6; Id. at 29, line 17 to 30, line 9; Figure 8). Discloses the use of glass and derivatized membrane supports (Id. at 21, lines 8-9).
23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting groups.	Discloses the use of photolabile *o*-nitrobenzyl linkers (Id. at 30, lines 6-7).
24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.	Discloses that phosphoramidite derivatives of 5-propynyl-dU can be prepared (Id. at 22, lines 23-24).
25. A method of detecting an oligonucleotide target comprising: enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids using an array of oligonucleotides on a solid support to capture complementary zip code tails on LDR

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
oligonucleotide analogue targets;	products (Id. at 11, lines 4-6). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary zip codes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9).
selecting said oligonucleotide analogue targets such that said oligonucleotide analogue targets bind to the complementary oligonucleotide probes coupled to a solid surface at known locations of an array with a similar hybridization stability across the array;	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44). Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A•T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
hybridizing the oligonucleotide analogue targets to complementary oligonucleotide probes; and	Discloses LDR products having a "zip code" tail, which hybridize to complementary zip codes on a solid support (Id. at 11, lines 5-6).
detecting whether at least one of said oligonucleotide analogue targets binds to said complementary oligonucleotide acid probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (Id. at 19, line 44, to 21, line 25; Figure 2).
26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10). Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10). Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA

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	duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
28. A method of making an array of oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
providing a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue,	Discloses DNA oligonucleotides or PNA oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9).
said oligonucleotide analogue probes having different sequences at known locations on an array, and	Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses PNA oligomers in unique addressable arrays (Id. at 21, lines 27-30). Discloses a PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
selecting the oligonucleotide analogue probes to hybridize with complementary oligonucleotide target sequences under hybridization conditions such that said oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44).
with a similar hybridization stability across the array.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
29. The method of claim 28, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences to increase and optimize T_m values (Id. at 11, lines 8-10). Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (Id. at 22, lines 20-21). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9 of description of Figure 5).
30. The method of claims 28 further comprising: incorporating a 5-propynyluracil base into the oligonucleotide analogue probes of the array.	Discloses the preparation of DNA or PNA synthetic probes, with either all thymine or all 5-propynyl-uracil (Id. at 22, lines 20-21; Id. at 23, lines 20-21).
31. The method of claim 28 further comprising: selecting said at least one oligonucleotide analogue such that oligonucleotide analogue probes comprises at least one peptide nucleic acid.	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8).
32. The method of claim 28 further comprising: providing said plurality of oligonucleotide analogue probes in an array with at least 1000 other oligonucleotide analogue probes.	Discloses a universal PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54; Id. at 31, lines 30-31).
33. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
a solid substrate and an array of a plurality of oligonucleotide analogue probes coupled to the solid substrate,	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9).
wherein the oligonucleotide analogue probes have different sequences and	Discloses PNA oligomers in unique addressable arrays (Id. at 21, lines 27-30). Discloses a PNA

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
are selected to hybridize to complementary oligonucleotide targets	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44).
under uniform hybridization conditions.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
34. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44). Discloses a plurality of different sequences attached at different locations (addresses) on a solid support (Id. at 19, lines 36-44). Discloses a universal PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54).
hybridized to complementary oligonucleotide analogue targets,	Discloses LDR products having a zip code tail which hybridize to complementary zip codes on a solid support where the complementary components are DNA or PNA (Id. at 11, lines 4-6). Replaces thymine with 5-propynyl uridine when used within DNA or PNA address sequences (complementary oligonucleotide probes) as well as in the DNA zip code sequences (Id. at 11, lines 8-10; Id. at 24, lines 8-9).

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
35. A method of analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids using an array of oligonucleotides on a solid support to capture complementary zip code tails on LDR products (Id. at 11, lines 4-6).
providing on a solid substrate an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences;	Discloses DNA oligonucleotides or PNA oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9). Discloses PNA oligomers in unique addressable arrays (Id. at 21, lines 27-30). Discloses a PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to complementary target oligonucleotides	Discloses contacting ligated reaction product with a solid support including complementary zip codes (DNA oligonucleotides or PNA oligomers) which are complementary to addressable array-specific portions (zip codes) of a ligated product sequence (Id. at 11, lines 4-7). The zip code tail of the ligated reaction product will be captured by a complementary zip code on the solid support (Id. at 11, lines 5-6). Discloses incorporation of the nucleotide analogue, 5-propynyl uridine, into DNA zip code and PNA address sequences (Id. at 11,

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	lines 8-10).
under uniform hybridization conditions; and	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (Id. at 19, line 44, to 21, line 25; Figure 2).
36. A method of detecting an oligonucleotide target comprising: enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids using an array of oligonucleotides on a solid support to capture complementary zip code tails on LDR products (Id. at 11, lines 4-6). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (complementary zip codes) as well as in the DNA zip code sequences (Id. at 24, lines 8-9).
providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44).
under uniform hybridization conditions;	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G•C/A T content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).
exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and	Discloses LDR products having a "zip code" tail, which hybridize to complementary zip codes on a solid support (Id. at 11, lines 5-6).
detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (Id. at 19, line 44, to 21, line 25; Figure 2).
37. A method of making an array of oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (Id. at 19, lines 36-44) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (see, e.g., Id. at 11, lines 4-6; Id. at 16, lines 1-14).
providing, on an array, a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences,	Discloses DNA oligonucleotides or PNA oligomers (complementary zip codes) attached at different locations to a solid support (Id. at 21, lines 27-30; Id. at 22, lines 9-10; Id. at 25, lines 5-8). Discloses that thymine can be replaced by 5-propynyl uridine when used within DNA or PNA address sequences (attached to a support) as well as in DNA zip code sequences (Id. at 24, lines 8-9). Discloses a plurality of DNA oligonucleotides or PNA oligomers attached to the solid support, each having different nucleotide sequences (Id. at 19, lines 36-44). Discloses PNA oligomers in unique addressable arrays (Id. at 21, lines 27-30). Discloses a PNA oligonucleotide array with 1,296 addresses (Id. at 21, lines 53-54). Discloses complementary zip code at discrete address on a two-dimensional array (Id. at 35, lines 16-18).
wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets	Discloses LDR products having a "zip code" tail, which will be selectively captured by a complementary zip code (DNA oligonucleotides or PNA oligonucleotides) on a solid support (Id. at 11, lines 4-7; Id. at 19, lines 42-44).
under uniform hybridization conditions.	Discloses that zip code (oligonucleotide) capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by LDR products having a zip code tail and the complementary zip codes (DNA or PNA oligonucleotides) on the solid support hybridized to one another resulting from differences in G C/A•T

Claims of the Present Application	Disclosure in the February 4, 1994 Grant Application
	content (Id. at 22, lines 18-20). Discloses narrowing the T_m difference between zip code/address duplexes and raising the T_m for all zip code/address duplexes (Id. at 22, lines 18-24). Discloses that the T_m for the correct PNA/DNA hybridization is at least 48 °C higher than any incorrect hybridization and neighboring 24-mers are separated by 12-mers, which do not hybridize with anything (Id. at 31, lines 23-25).

D. Grant Application – Details Regarding Review

As described above, the Grant Application was submitted to NCI by, amongst others, Francis Barany, Donald Bergstrom, and co-inventors George Barany and Robert Hammer on or before February 4, 1994 (Barany Declaration ¶ 5). Such a submission is confirmed by Cornell Medical College's files of grant applications submitted, which include a grant application, entitled "New Methods for Cancer Detection" ("Grant Application"), which was submitted to the National Cancer Institute, U.S. Department of Health and Human Services ("NCI") by, amongst others, Francis Barany of Cornell Medical College on February 4, 1994 (see Declaration of Gregory W. Siskind Under 37 CFR § 1.608(b) ("Siskind Declaration") ¶ 4).

As set forth in the Barany Declaration, on May 31, 1994 to June 2, 1994, the NCI Site Special Review Subcommittee for the Grant Application visited Cornell University Medical College, New York, New York to meet with the scientists who submitted the Grant Application, including Francis Barany, Donald Bergstrom, and co-inventors George Barany and Robert Hammer (Barany Declaration ¶ 17). As indicated in the follow-up July 20-22, 1994, Draft Review Report (attached as Appendix 2 to the Barany Declaration) regarding the Grant Application, the NCI Site Special Review Subcommittee included Steven P.A. Fodor, Ph.D., Scientific Director and Chief Technical Officer of Affymetrix, Inc., Santa Clara, California (Appendix 2 of the Barany Declaration at p. 32), who was in attendance at the site visit (Barany Declaration ¶ 17).

E. U.S. Patent No. 6,156,501 – Filing Details

In the '501 patent, Glenn Hugh McGall, Charles Garrett Miyada, Maureen T. Cronin, Jennifer Dee Tan, and Mark S. Chee ("McGall et al.") are named inventors and Affymetrix, Inc. ("Affymetrix") is the assignee. U.S. Patent Application Serial No. 08/630,427 ("the '427 application")) which issued as the '501 patent, was filed on April 3, 1996. The '427 application is a continuation-in-part of U.S. Patent Application Serial No. 08/440,742 ("the '742 application"), filed May 10, 1995, which is a continuation-in-part of PCT Application No. PCT/US94/12305 (which includes Steven P.A. Fodor as an inventor). The PCT application had been filed on October 26, 1994, and is a continuation-in-part of U.S. Application Serial No. 08/284,064 (which includes Steven P.A. Fodor as an inventor), filed August 2, 1994, now abandoned, which, in turn, is a continuation-in-part of U.S. Application Serial No. 08/143,312 (which includes Steven P.A. Fodor as an inventor), filed October 26, 1993, now abandoned. All claims of the '501 patent require oligonucleotide analogues as well as an array of oligonucleotide probes which are selected to bind to complementary oligonucleotide targets with a similar hybridization stability across the array. The first disclosure relating to oligonucleotide analogue arrays in the above-described chain of applications is found in the October 26, 1994, PCT application, however, there was no disclosure relating to binding to complementary oligonucleotide targets with a similar hybridization stability across the array until, at the earliest, May 10, 1995, when the '742 application was filed. This was recognized by the U.S. Patent and Trademark Office ("PTO") during prosecution of the '742 application, when the PTO indicated that the claimed oligonucleotide analogue arrays were only entitled to the May 10, 1995, filing date of the '742 application ("[c]onsideration of the instant claims has resulted in noting that they contain limitations that were disclosed first in the instant application and thus are granted priority only to 5/10/95"). Applicants question whether the claims of the '501 patent are even entitled to a filing date of May 10, 1995, but, in any event, this is clearly the earliest date that the claims are entitled to.

II. The Claimed Invention Of The '501 Patent Was Derived From Applicants

A. Applicable Law

A claim of derivation of an invention addresses originality – who invented the subject matter? Price v. Symsek, 988 F.2d 1187, 1190, 26 USPQ2d 1031, 1033 (Fed. Cir. 1993). A party alleging derivation asserts that the opposing party did not "invent" the subject matter, because the opposing party derived the invention from another. Id. In proving derivation, a party must establish: (1) prior conception of the claimed subject matter; and (2) communication of the conception to the adverse claimant. Id. The party alleging derivation must first show a complete conception of the claimed subject matter (or subject matter of the count) prior to the conception by the opposing party. Mead v. McKirnan, 585 F.2d 504, 507, 199 USPQ 513, 515 (CCPA 1978); Goeddel v. Weissman, 1995 Pat. App. LEXIS 10 at *46 (Bd. Pat. App. & Interf. December 15, 1995). Conception is complete when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation. Goeddel, 1995 Pat. App. LEXIS 10, at *46-47; Rhodes v. Dugan, 212 USPQ 699, 701-702 (Bd. Pat. App. & Interf. 1981) ("The test . . . for a complete conception and/or communication is that it 'must be sufficient to enable one of ordinary skill in the art to construct and successfully operate the invention.'" (citation omitted)).

In addition, there must be a communication of the complete conception prior to the corroborated conception date of the party charged with derivation. Tropix, Inc. v. Lumigen, Inc., 2000 Pat. App. LEXIS 7 (February 28, 2000). Further, the subject matter communicated must have been sufficient to enable one of ordinary skill in the art to construct and successfully operate the invention. Mead, 585 F.2d at 507, 199 USPQ at 515; Goeddel, 1995 Pat. App. LEXIS 10 at *46-47; English v. Ausnit, 38 USPQ2d 1625, 1637 (Bd. Pat. App. & Interf. 1993); Rhodes, 212 USPQ at 701.

B. Analysis

1. Applicants Conceived Of The Present Invention Well Before The Earliest Effective Filing Date Of The '501 Patent

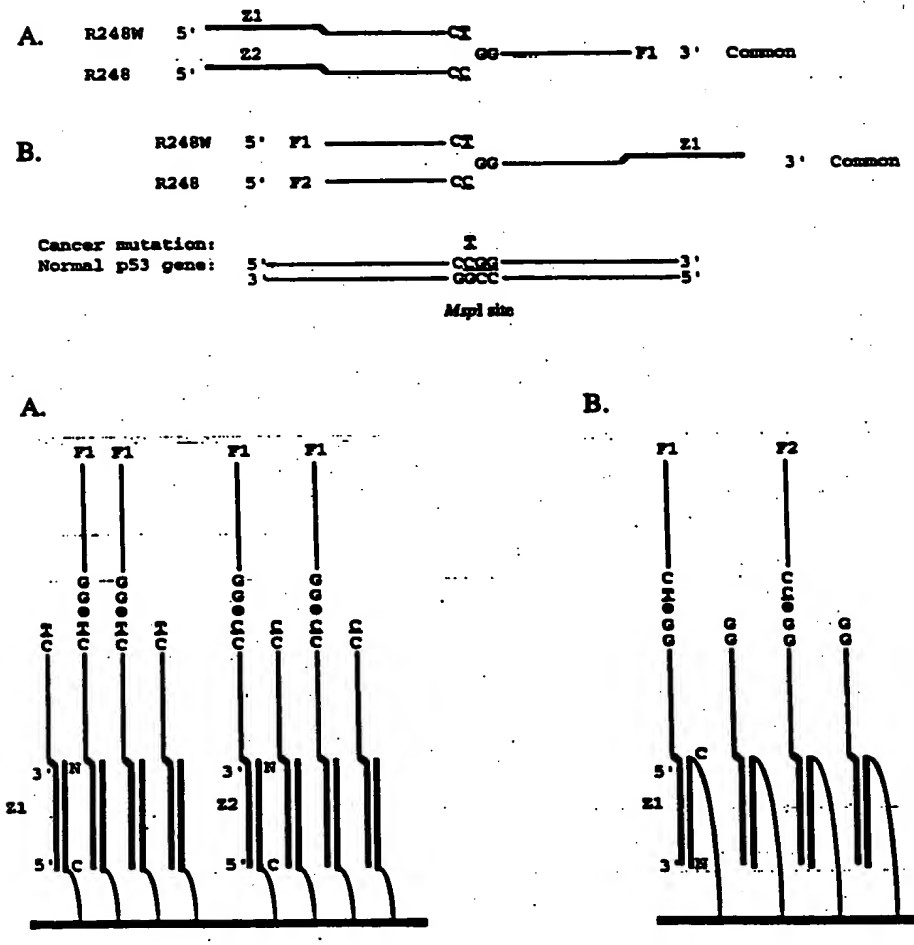
As set forth in the attached Barany Declaration and the attached Declaration of Donald Bergstrom Under 37 CFR § 1.608(b) ("Bergstrom Declaration"), on or before February 4, 1994, Francis Barany, George Barany, and Robert Hammer ("Barany et al.") formed a complete conception of the idea of using an array of a plurality of oligonucleotide analogue probes coupled to a solid support where the probes bind to complementary oligonucleotide targets with similar hybridization stability across the array (as claimed in the present application and the '501 patent). This was well before the earliest effective filing date of the '501 patent.

As described above, on or before February 4, 1994, a grant application, entitled "New Methods for Cancer Detection" ("Grant Application"), was submitted to NCI by, amongst others, Francis Barany, Donald Bergstrom, and co-inventors George Barany and Robert Hammer (Barany Declaration ¶ 5; Bergstrom Declaration ¶ 4).

The Grant Application describes five (5) projects, including Project 5, entitled "Design and Synthesis of DNA and PNA Arrays" (Barany Declaration ¶ 5; Siskind Declaration ¶ 4; Bergstrom Declaration ¶ 4). A copy of relevant portions of the Grant Application, including the Project 5 description, is attached as Appendix 1 to the Barany Declaration, the Siskind Declaration, and the Bergstrom Declaration (Barany Declaration ¶ 5; Siskind Declaration ¶ 4; Bergstrom Declaration ¶ 4).

Project 5 describes a method of detecting nucleic acid sequence differences in target nucleic acids by the use of a solid support with an array of peptide nucleotide analogues ("PNA") to capture and detect the products of a ligase detection reaction ("LDR") (Appendix 1 of Barany Declaration, p. 19-22) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5; Declaration of Gerald Zon under 37 CFR §1.608 ("Zon Declaration") ¶ 6). In particular, each ligation product of the LDR process is provided with a "zip code" tail (e.g., Z1 and Z2) which is selectively captured by a complementary "zip code" located at a particular "address" on the solid support (Id.) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5). As shown below, different target nucleic acids captured in this manner are detected and distinguished from one another by the presence of labels immobilized at different addresses on the array (having "zip code" capture probes with different nucleotide

sequences) or by the presence of different labels immobilized on the array (Id. at 22) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5).



The Grant Application discloses that the array "zip code" capture probes on the solid support can be designed to achieve optimal hybridization to the "zip code" tail on the ligation product (Id.) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5). This is achieved by increasing thermal stability through reduction of the difference in melting temperature (i.e. T_m) between the different duplexes formed by LDR products having a "zip code" tail and the complementary "zip codes" (i.e. PNA oligonucleotides) hybridized to one another on the solid support (Id.) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5). These differences in melting temperature result from differences in G•C/A•T content (Id.) (Barany Declaration

¶ 6; Bergstrom Declaration ¶ 5). The Grant Application states that the T_m for correct PNA/DNA hybridization is at least 48°C higher than for any incorrect hybridization and neighboring 24-mer capture probes on the solid support are separated by 12-mer oligonucleotides which do not hybridize to anything (Id. at 31) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5). The Grant Application also states that analogues with thymine replaced with 5-propynyl uridine can be used in either complementary zip codes (DNA or PNA) on the solid support or zip code (DNA) tails on the ligation product (Id. at 24) (Barany Declaration ¶ 6; Bergstrom Declaration ¶ 5).

Thus, Barany et al. formed a complete conception of DNA oligonucleotide or PNA oligomer arrays and their use in methods of detection of nucleic acid sequence differences in nucleic acids, as claimed and disclosed in the present application and the '501 patent, at least as early as February 1994. This was over one year before the May 10, 1995, potential effective filing date of McGall et al.

As set forth in the Barany Declaration and the Bergstrom Declaration, on May 31, 1994 to June 2, 1994, the NCI Site Special Review Subcommittee for the Grant Application visited Cornell University Medical College, New York, New York to meet with the scientists who submitted the Grant Application, including Francis Barany, Donald Bergstrom, and co-inventors George Barany and Robert Hammer (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7). As indicated in the follow-up July 20-22, 1994, Draft Review Report (attached as Appendix 2 to the Barany Declaration and the Bergstrom Declaration) regarding the Grant Application, the NCI Site Special Review Subcommittee included Steven P.A. Fodor, Ph.D., Scientific Director and Chief Technical Officer of Affymetrix, Inc., Santa Clara, California (Appendix 2 of the Barany Declaration/Bergstrom Declaration at p. 32), who was in attendance at the site visit (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7). Dr. Fodor's presence at the site visit (as well as on the review subcommittee) caused a great deal of concern amongst Francis Barany and Donald Bergstrom (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7). Having served on a number of NCI site review subcommittees, it was the understanding of Francis Barany and Donald Bergstrom that subcommittee members should not review grant applications where they have a conflict of interest or the appearance of one (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7). For example, where a subcommittee member has a financial interest in work closely related or competing with the subject matter of the grant application, a conflict of interest arises and that subcommittee member should not participate in deliberations and actions on the grant application (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7; Zon Declaration ¶ 5).

Since it was well known at the time of the site visit that Affymetrix was developing oligonucleotide arrays for the use of detecting single base mutations, Francis Barany and Donald Bergstrom wondered why Dr. Fodor did not remove himself from the review subcommittee (Barany Declaration ¶ 17; Bergstrom Declaration ¶ 7). Likewise, Dr. Fodor's fellow member of the NCI Site Special Review Subcommittee harbored similar concerns and recalls thinking "What is he doing here?" (Zon Declaration § 5).

Prior to the site visit, Francis Barany and Donald Bergstrom expressed their concern about Dr. Fodor's presence at the site visit to NCI; however, with assurance by NCI that it would guard against conflict of interest problems, Dr. Fodor remained on the review subcommittee (Barany Declaration ¶ 18; Bergstrom Declaration ¶ 8). Francis Barany and Donald Bergstrom continued to be concerned about Dr. Fodor's presence on the subcommittee and, after learning of work subsequently presented by Affymetrix scientists, sent a letter on November 11, 1994, to Dr. James Jacobson of NCI (attached to the Barany Declaration and Bergstrom Declaration at Appendix 3), in which Francis Barany and Donald Bergstrom again protested the presence of Dr. Fodor on the site review subcommittee on the grounds that he may have had a conflict of interest (Barany Declaration ¶ 18; Bergstrom Declaration ¶ 8).

Since the Grant Application embodies the complete conception of the design and synthesis of DNA and PNA arrays, it is clear that applicants' invention was communicated to Dr. Fodor at least as early as May 31, 1994 to June 2, 1994. This was almost one year prior to May 10, 1995, potential effective filing date of the '501 patent.

In the present case, a communication from Dr. Fodor to the inventors of the '742 application (which later issued as the '501 patent) should be inferred from Dr. Fodor's position at Affymetrix. In particular, Dr. Fodor was Scientific Director and Chief Technical Officer of Affymetrix, as shown in the Draft Review Report attached to the Barany Declaration and the Bergstrom Declaration at Appendix 2. In addition, Dr. Fodor was listed as an inventor for many patent applications for Affymetrix. In particular, Dr. Fodor was listed as an inventor on all patent applications in the chain leading up to the '501 patent, except the application which issued into the '501 patent (the '427 application) and its parent application (the '742 application")) (see Section I.E., *supra*). Therefore, it is apparent that Dr. Fodor was significantly involved in the preparation and filing of patent applications for Affymetrix. In addition, the sequence of events relating to this matter strongly suggest that Dr. Fodor communicated the invention of the Grant Application to the inventors at the '501 patent. The first disclosure relating to oligonucleotide analogue arrays in the chain of

applications leading up to the '501 patent is found in the October 26, 1994, PCT application, which lists Dr. Fodor as an inventor. The October 26, 1994, PCT application was filed after Dr. Fodor's review of the Grant Application. The first disclosure relating to binding to a complementary oligonucleotide target with a similar hybridization stability across the array is at best found in the '742 application, which was also filed after Dr. Fodor's review of the Grant Application. For all of these reasons, there is a high likelihood that the information received by Dr. Fodor when reviewing the Grant Application was communicated to the inventors of the '501 patent.

Applicants have shown: (1) prior conception of the claimed subject matter; and (2) communication of the conception to the inventors of the '501 patent. In view of this *prima facie* showing that applicants are entitled to a judgment over McGall et al., because the claimed invention was derived from applicants, an interference should be declared.

III. The Subject Matter Of The '501 Patent Is Not Patentable To The Inventors of the '501 Patent Under 35 U.S.C. §§ 102(f) or 103(a)

A. Applicable Law

Under 35 U.S.C. § 102(f) (2001), a person shall be entitled to a patent unless – "he did not himself invent the subject matter sought to be patented." The originality requirement of 35 U.S.C. § 102(f) means that a person cannot obtain a patent on an invention if he obtained an idea for the invention from another source. To invalidate a patent for derivation of invention under 35 U.S.C. § 102(f), "a party must demonstrate that the inventor[s] of the patent acquired knowledge of the claimed invention from another, or at least so much of the claimed invention as would have made it obvious to one of ordinary skill in the art." New England Braiding Co., Inc. v. A.W. Chesterton Co., 970 F.2d 878, 883, 23 USPQ2d 1622, 1626 (Fed. Cir. 1992). Under 35 U.S.C. § 102(f), prior private or secret information of which an applicant had actual knowledge would be available against him. OddzOn Products, Inc. v. Just Toys, Inc., 122 F.3d 1396, 1401-1402, 43 USPQ2d 1641, 1644 (Fed. Cir. 1997); Ex parte Stalego, 154 USPQ 52, 53 (Pat. & Tm. Off. Bd. App. 1966); Ex parte Thelin, 152 USPQ 624, 625 (Pat. & Tm. Off. Bd. App. 1966).

B. Analysis

As described above, Steven P.A. Fodor reviewed and had access to the Grant Application by Barany et al. at least about one year prior to the filing date of the '742 application. The '742 application is the first application in the chain of applications leading up to the '501 patent to contain any disclosure relating to binding to a complementary oligonucleotide target with a similar hybridization stability across an oligonucleotide analogue array.

As noted *supra*, a communication of the subject matter of the Grant Application from Dr. Fodor to the inventors of the '742 application (which later issued as the '501 patent) should be inferred based on Dr. Fodor's position as Scientific Director and Chief Technical Officer of Affymetrix and Dr. Fodor's status as an inventor for all related applications prior to the '742 application. The timing of events also strongly suggests that Dr. Fodor communicated the subject matter of the Grant Application to the inventors of the '742 application. In particular, the first disclosure relating to oligonucleotide analogue arrays in the chain of applications leading up to the '501 patent is found in the October 26, 1994, PCT application, which lists Dr. Fodor as an inventor and was filed after Dr. Fodor's review of the Grant Application. For all these reasons, there is good reason to believe that the information received by Dr. Fodor when reviewing the Grant Application was communicated to the inventors of the '501 patent.

Accordingly, the Grant Application was prior art under 35 U.S.C. §§ 102(f) or 103(a) with respect to the '501 patent and, therefore, the subject matter of the '501 patent is not patentable to the inventors of the '501 patent.

IV. The Subject Matter Of The '501 Patent Is Not Patentable To The Inventors Of The '501 Patent Due To Inequitable Conduct

A. Applicable Law

Under 37 CFR § 1.56(a) (2001), "[e]ach individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability . . . ." Individuals associated with the filing or prosecution of a patent application include: (1) each inventor; (2) each attorney or agent who

prepares or prosecutes the application; and (3) every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, the assignee, or with anyone obligated to assign the application. 37 CFR § 1.56(c) (2001). A breach of that duty constitutes inequitable conduct. Inequitable conduct resides in the failure to disclose material information with an intent to deceive. Ruiz v. A.B. Chance, Co., 234 F.3d 654, 670, 57 USPQ2d 1161, 1171 (Fed. Cir. 2000) (citation omitted).

B. Analysis

Based on the facts as described above, the inventors of the '501 patent and/or Dr. Fodor committed inequitable conduct by failing to disclose, to the U.S. Patent and Trademark Office ("PTO"), during prosecution of the '427 application or the '742 application, their knowledge about the Grant Application by Barany et al. and the prior conception of using oligonucleotide analogue/PNA arrays by Barany et al. As noted above, Dr. Fodor had access to the Grant Application at least during the period between May 31, 1994 and June 2, 1994, so he knew of the prior conception of using oligonucleotide analogue/PNA arrays by Barany et al. while the '427 application and the '742 application were pending. As noted above, it should be inferred that the information contained within the Grant Application was communicated to others at Affymetrix, including the inventors of the '427 application and the '742 application (which later issued as the '501 patent), due to the position of Dr. Fodor at Affymetrix, his status as inventor in the ancestor cases, and the timing of various events. Since this use of oligonucleotide analogue arrays to achieve hybridization stability across an array is the subject matter of what issued as the '501 patent, the fact that someone else made this invention would have been highly material to the PTO. Likewise, the failure by the inventors of the '501 patent to disclose this information to the PTO can only be regarded as an act of deceptive intent. Therefore, the inventors of the '501 patent and/or Dr. Fodor committed inequitable conduct during prosecution of the '501 patent by failing to disclose to the PTO their knowledge of the Grant Application.

Accordingly, the subject matter of the '501 patent is not patentable to the inventors of the '501 patent.

V. The Claims Of The Present Application Are Entitled To A Filing Date Of February 9, 1996.

Claims 1-37 of the present application, which correspond to the proposed count, are descriptively supported by the original disclosure of the present application as follows:

Claims of the Present Application	Descriptive Support in the Present Application
1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 12, 33, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide analogue probes having different sequences,	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37). Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 12, 33, and 34).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 12, 33, and 34).
wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed

Claims of the Present Application	Descriptive Support in the Present Application
	by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G C/A T content (page 35, lines 12-15).
2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.	Discloses an array of oligonucleotides on a solid support with at least some of the array portions being occupied by oligonucleotides having greater than 16 nucleotides (page 7, lines 25-27). Discloses a 20 mer capture oligonucleotide (page 45, lines 17-18). Discloses assembling arrays with tetramers to produce capture oligonucleotides up to 24 nucleotides in length (page 38, line 20 to page 48, line 21).
5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (page 40, lines 35-37).
6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 8-10).
7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23).
9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to

Claims of the Present Application	Descriptive Support in the Present Application
synthesis of said plurality of oligonucleotide analogue probes.	page 27, line 2; page 50, line 17 to page 51, line 6).
10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to page 27, line 2; page 50, line 17 to page 51, line 6).
12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 33, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (see, e.g., claim 34). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-36). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared	Discloses that oligonucleotides (normal and complementary directions, for capture hybridization) are prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 13, line 38 to page 14, line 2 and page 35,

Claims of the Present Application	Descriptive Support in the Present Application
to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	lines 1-10). Such analogues pair with perfect complementarity to the natural bases but increase T_m values (e.g., 5-propynyl-uracil) (page 40, lines 37-38).
14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support (see, e.g., claims 25, 35, and 36).
(a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-15; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (see, e.g., claims 1, 12, 33, and 34).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations,	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (see, e.g., claims 1, 12, 33, and 34).
said solid substrate having a surface;	Discloses a solid support having a substrate and a surface (page 25, lines 18-26).
(b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide

Claims of the Present Application	Descriptive Support in the Present Application
	capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
(c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
16. The method of claim 15, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.	Discloses the use of a DNA sample (page 12, lines 13-14 and 38-39).
18. The method of claim 15, wherein said target nucleic acid is amplified prior to said hybridization step.	Discloses that sample is amplified during the ligase detection reaction and prior to hybridization to oligonucleotide probes (page 15, lines 1-17; page 20, lines 5-12).
19. The method of claim 15, wherein said plurality of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23).
20. The method of claim 15, wherein said plurality of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
22. The method of claim 15, wherein said solid substrate is comprised of materials selected from the group consisting of silica, polymers and glass.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5).
23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23).

Claims of the Present Application	Descriptive Support in the Present Application
groups.	
24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.	Discloses that phosphoramidite derivatives of 5-propynyl-dU can be prepared (page 35, lines 21-27).
25. A method of detecting an oligonucleotide target, comprising	Discloses an array of oligonucleotides on a solid support (claims 1, 12, 33, and 34)) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids (claims 15, 35, and 36).
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets,	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 29 to page 11, line 10). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 5-7).
selecting said oligonucleotide analogue targets such that said oligonucleotide analogue targets bind to the complementary oligonucleotide probes coupled to a solid surface at known locations of an array	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
hybridizing the oligonucleotide analogue targets to complementary oligonucleotide probes; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the

Claims of the Present Application	Descriptive Support in the Present Application
	capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
detecting whether at least one of said oligonucleotide analogue targets binds to said complementary oligonucleotide acid probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37) which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33). The ligated product sequence can be prepared with oligonucleotide probes which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
28. A method of making an array of oligonucleotide probes, comprising	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 13-14).
providing a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
said oligonucleotide analogue probes having different sequences at known locations on an array, and	Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1 and 33). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions

Claims of the Present Application	Descriptive Support in the Present Application
	(claims 1 and 33).
selecting the oligonucleotide analogue probes to hybridize with complementary oligonucleotide target sequences under hybridization conditions such that said oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
29. The method of claim 28, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
30. The method of claim 28 further comprising: incorporating a 5-propynyluracil base into the oligonucleotide analogue probes of the array.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
31. The method of claim 28 further comprising: selecting said at least one oligonucleotide analogue such that oligonucleotide analogue probes comprises at least one peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNA), with either natural bases or nucleotide analogues (page 40, lines 35-37).
32. The method of claim 28 further comprising: providing said plurality of oligonucleotide analogue probes in an array with at least 1000 other oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 8-10).
33. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
a solid substrate and an array of a plurality of oligonucleotide analogue probes coupled to the	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to a

Claims of the Present Application	Descriptive Support in the Present Application
solid substrate,	solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 1, 12, and 34).
wherein the oligonucleotide analogue probes have different sequences and	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1, 12, and 34).
are selected to hybridize to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
34. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, and 33) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (see, e.g., claim 12). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37).
hybridized to complementary oligonucleotide	Discloses capture oligonucleotides which are

Claims of the Present Application	Descriptive Support in the Present Application
analogue targets,	complementary to addressable array-specific portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-36). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
35. A method of analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support (see, e.g., claims 15, 25, and 36).
providing on a solid substrate an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences;	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-15; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (see, e.g., claims 1, 12, 33, and 34). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (see, e.g., claims 1, 12, 33, and 34).
exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence

Claims of the Present Application	Descriptive Support in the Present Application
complementary target oligonucleotides	containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
36. A method of detecting an oligonucleotide target comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, 33, and 34)) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids (claims 15, 25, and 36).
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 29 to page 11, line 10). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 5-7).
providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).

Claims of the Present Application	Descriptive Support in the Present Application
under uniform hybridization conditions;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
37. A method of making an array of oligonucleotide probes comprising:	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 13-14).
providing, on an array, a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1 and 33). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 1 and 33).
wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c)

Claims of the Present Application	Descriptive Support in the Present Application
	the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).

In addition, claims 1-37 of the present application are descriptively supported by the original disclosure of the parent application as follows:

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide analogue probes having different sequences,	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 33-35). Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.	Discloses an array of oligonucleotides on a solid support with at least some of the array positions being occupied by oligonucleotides having greater than 16 nucleotides (page 7, lines 23-25). Discloses a 20 mer capture oligonucleotide (page 45, lines 17-18). Discloses assembling arrays with tetramers to produce capture oligonucleotides up to 24 nucleotides in length (page 38, line 20 to page 48, line 21).
5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (page 40, lines 35-37).

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
analogues comprises a peptide nucleic acid.	
6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 7-9).
7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23). Discloses forming an array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to page 27, line 2; page 50, line 17 to page 51, line 6).
10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to page 27, line 2; page 50, line 17 to page 51, line 6).
12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (claim 120). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 33-35).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6,

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
	lines 36-40; page 11, lines 3-5). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, lines 35-38).
wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses that oligonucleotides (normal and complementary directions, for capture hybridization) are prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 13, lines 35-38 and page 35, lines 1-10). Such analogues pair with perfect complementarity to the natural bases but increase T_m values (e.g., 5-propynyl-uracil) (page 40, lines 37-38).
14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support (see, e.g., claim 1).
(a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 33-35). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations,	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
said solid substrate having a surface;	Discloses a solid support having a substrate and a surface (page 25, lines 17-26).
(b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
with a similar hybridization stability across the array; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
(c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 19-21).
16. The method of claim 15, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.	Discloses the use of a DNA sample (page 12, lines 11 and 36).
18. The method of claim 15, wherein said target nucleic acid is amplified prior to said hybridization step.	Discloses that sample is amplified during the ligase detection reaction and prior to hybridization to oligonucleotide probes (page 14, line 39 to page 15, line 15, page 20, lines 3-10).
19. The method of claim 15, wherein said plurality of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23). Discloses forming an array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
20. The method of claim 15, wherein said plurality	Discloses application of solution including 5'

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of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.	amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 17-33; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
22. The method of claim 15, wherein said solid substrate is comprised of materials selected from the group consisting of silica, polymers and glass.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 17-33; page 26, lines 1-5).
23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting groups.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23). Discloses forming an array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.	Discloses that phosphoramidite derivatives of 5-propynyl-dU can be prepared (page 35, lines 21-27).
25. A method of detecting an oligonucleotide target, comprising	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids.
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 27 to page 11, line 8). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, lines 35-38) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 3-5).
selecting said oligonucleotide analogue targets such that said oligonucleotide analogue targets bind to	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
the complementary oligonucleotide probes coupled to a solid surface at known locations of an array	portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
with a similar hybridization stability across the array;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
hybridizing the oligonucleotide analogue targets to complementary oligonucleotide probes; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
detecting whether at least one of said oligonucleotide analogue targets binds to said complementary oligonucleotide acid probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 19-21).
26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37) which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6,

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
	lines 36-40; page 11, lines 3-5). The ligated product sequence can be prepared with oligonucleotide probes which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, lines 35-38).
28. A method of making an array of oligonucleotide probes, comprising	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 11-12).
providing a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 33-35). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
said oligonucleotide analogue probes having different sequences at known locations on an array, and	Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
selecting the oligonucleotide analogue probes to hybridize with complementary oligonucleotide target sequences under hybridization conditions such that said oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40, page 11, lines 3-5).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
29. The method of claim 28, wherein at least one	Discloses the use of 5-propynyl uridine in place of

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of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
30. The method of claim 28 further comprising: incorporating a 5-propynyluracil base into the oligonucleotide analogue probes of the array.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
31. The method of claim 28 further comprising: selecting said at least one oligonucleotide analogue such that oligonucleotide analogue probes comprises at least one peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNA), with either natural bases or nucleotide analogues (page 40, lines 35-37).
32. The method of claim 28 further comprising: providing said plurality of oligonucleotide analogue probes in an array with at least 1000 other oligonucleotide an probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 7-9).
33. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
a solid substrate and an array of a plurality of oligonucleotide analogue probes coupled to the solid substrate,	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to a solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
wherein the oligonucleotide analogue probes have different sequences and	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 33-35). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
are selected to hybridize to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c)

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	the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
34. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (claim 120). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 33-35).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, lines 35-38).
wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G C/A T content (page 35, lines 12-15).
35. A method of analyzing interactions between	Discloses a method for detecting nucleic acid

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oligonucleotide targets and oligonucleotide probes comprising:	sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support (see, e.g., claim 1).
providing on a solid substrate an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences;	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 33-35). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to complementary target oligonucleotides	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
under uniform hybridization conditions; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 19-21).
36. A method of detecting an oligonucleotide target comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in

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	target nucleic acids.
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 27 to page 11, line 8). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, lines 35-38) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 3-5).
providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
under uniform hybridization conditions;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 19-21).

Claims of the Present Application	Descriptive Support in U.S. Patent Application Serial No. 08/794,851 ("parent application")
37. A method of making an array of oligonucleotide probes comprising:	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 11-12).
providing, on an array, a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 33-35). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-33). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 35-36). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 36-40; page 11, lines 3-5).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).

Moreover, claims 1-37 of the present application are descriptively supported by the original disclosure of the grandparent application as follows:

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide analogue probes having different sequences,	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 12, lines 15-17). Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 37, lines 7-13; page 42, lines 10-15). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	with increased T_m values (page 43, lines 3-4).
3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 26, line 26 to page 27, line 4; page 27, lines 11-15). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 52, lines 32-36).
4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.	Discloses an array of oligonucleotides on a solid support with at least some of the array portions being occupied by oligonucleotides having greater than 16 nucleotides (page 7, lines 31-33). Discloses a 20 mer capture oligonucleotide (page 47, lines 33-34). Discloses assembling arrays with tetramers to produce capture oligonucleotides up to 24 nucleotides in length (page 40, line 24 to page 51, line 4).
5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (page 43, lines 1-3).
6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 25, lines 14-16).
7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 38, lines 8-16).
8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.	Discloses the use of positive/negative light reactive protective groups (page 32, line 33 to page 34, line 8). Discloses forming array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 28, lines 11-14; page 53, lines 3-33).
10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are	Discloses application of solution including 5' amino-modified oligonucleotide to the solid

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.	support using a prefabricated mask (page 54, line 31 to page 55, line 3).
11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 28, lines 11-14; page 53, lines 3-33).
12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (claim 120). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 12, lines 15-17).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 14, lines 21-24).
wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide	Discloses that oligonucleotides (normal and complementary directions, for capture hybridization) are prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 14, lines 21-24 and page 36, line 30 to page 37, line 2). Such analogues pair with perfect complementarity to the natural bases but increase

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
probe with which said oligonucleotide analogue target anneals.	T_m values (e.g., 5-propynyl-uracil) (page 43, lines 3-4).
14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3).
15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support to capture (see, e.g., claim 1).
(a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 12, lines 15-17). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations,	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
said solid substrate having a surface;	Discloses a solid support having a substrate and a surface (page 26, lines 26-35).
(b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
with a similar hybridization stability across the array; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
	between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
(c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 17-19).
16. The method of claim 15, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 37, lines 7-13; page 42, lines 10-15). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 43, lines 3-4).
17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.	Discloses the use of a DNA sample (page 12, line 33 and page 13, line 20).
18. The method of claim 15, wherein said target nucleic acid is amplified prior to said hybridization step.	Discloses that sample is amplified during the ligase detection reaction and prior to hybridization to oligonucleotide probes (page 15, line 25 to page 16, line 3, page 21, lines 3-10).
19. The method of claim 15, wherein said plurality of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.	Discloses the use of positive/negative light reactive protective groups (page 32, line 33 to page 34, line 8). Discloses forming array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
20. The method of claim 15, wherein said plurality of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 54, line 31 to page 55, line 3).
21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 26, line 26 to page 27, line 4; page 27, lines 11-15). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 52, lines 32-36).
22. The method of claim 15, wherein said solid substrate is comprised of materials selected from the group consisting of silica, polymers and glass.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as

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	particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 26, line 26 to page 27, line 4; page 27, lines 11-15).
23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting groups.	Discloses the use of positive/negative light reactive protective groups (page 32, line 33 to page 34, line 8). Discloses forming array of capture oligonucleotides using photolithographic masking and photochemical deprotection of linkers to add nucleotides with a photoactivatable protecting group (claim 105).
24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.	Discloses that phosphoramidite derivatives of 5-propynyl-dU can be prepared (page 37, lines 13-19).
25. A method of detecting an oligonucleotide target comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids.
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 11, lines 7-28). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 14, lines 21-24) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 23-25).
selecting said oligonucleotide analogue targets such that said oligonucleotide analogue targets bind to the complementary oligonucleotide probes coupled to a solid surface at known locations of an array	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
with a similar hybridization stability across the array;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture

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	oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
hybridizing the oligonucleotide analogue targets to complementary oligonucleotide probes; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
detecting whether at least one of said oligonucleotide analogue targets binds to said complementary oligonucleotide acid probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 17-19).
26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 37, lines 7-13; page 42, lines 10-15). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 43, lines 3-4).
27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3) which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25). The ligated product sequence can be prepared with oligonucleotide probes which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 14, lines 21-24).
28. A method of making an array of oligonucleotide probes comprising:	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 19-21).
providing a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 12, lines 15-17). Discloses attaching

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
	DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3).
said oligonucleotide analogue probes having different sequences at known locations on an array, and	Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
selecting the oligonucleotide analogue probes to hybridize with complementary oligonucleotide target sequences under hybridization conditions such that said oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
29. The method of claim 28, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl uridine in place of thymine to increase the thermal stability of DNA duplexes (page 37, lines 7-13; page 42, lines 10-15). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 43, lines 3-4).
30. The method of claim 28 further comprising: incorporating a 5-propynyluracil base into the oligonucleotide analogue probes of the array.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
	strands to be linked to a solid support (page 38, lines 8-16).
31. The method of claim 28 further comprising: selecting said at least one oligonucleotide analogue such that oligonucleotide analogue probes comprises at least one peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNA), with either natural bases or nucleotide analogues (page 43, lines 1-3).
32. The method of claim 28 further comprising: providing said plurality of oligonucleotide analogue probes in an array with at least 1000 other oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 25, lines 14-16).
33. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
a solid substrate and an array of a plurality of oligonucleotide analogue probes coupled to the solid substrate,	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
wherein the oligonucleotide analogue probes have different sequences and	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 12, lines 15-17). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80).
are selected to hybridize to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
	narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
34. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array.
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (claim 120). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 12, lines 15-17).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 14, lines 21-24).
wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
35. A method of analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support to capture (see, e.g., claim 1).
providing on a solid substrate an oligonucleotide analogue array comprising a plurality of	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
oligonucleotide analogue probes having different sequences;	support (page 12, lines 15-17). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to complementary target oligonucleotides	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
under uniform hybridization conditions; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 17-19).
36. A method of detecting an oligonucleotide target comprising:	Discloses an array of oligonucleotides on a solid support (claim 120) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids.
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
targets;	(ligation phase) (page 11, lines 7-28). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 14, lines 21-24) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 23-25).
providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
under uniform hybridization conditions;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).
exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 17-19).
37. A method of making an array of oligonucleotide probes comprising:	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 19-21).
providing, on an array, a plurality of	Discloses attaching a plurality of different capture

Claims of the Present Application	Descriptive Support in U.S. Provisional Patent Application Serial No. 60/011,359 ("grandparent application")
oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences,	oligonucleotides at different locations on a solid support (page 12, lines 15-17). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 21-24; page 32, lines 14-15). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 43, lines 1-3). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claim 80). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 7, lines 3-4). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claim 124).
wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 7, lines 4-8; page 11, lines 20-25).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 51, line 37 to page 52, line 1). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 37, lines 4-7).

Thus, the claims of the present application are entitled to the February 9, 1996, filing date of the grandparent application.

VI. Conclusion

In view of applicants' demonstration that their invention was derived by the inventors of the '501 patent and that the subject matter of the '501 patent is not patentable to the inventors of the '501 patent, an interference should be declared between the present application and the '501 patent.

Respectfully submitted,

Date: January 7, 2002

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Jan 7, 2002 — Date

Ruth R. Smith — Ruth R. Smith

PATENT
Docket No.: **19603/3357 (CRF D-1595)**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants	:	Barany et al.	Examiner: To Be Assigned
Serial No.	:	09/986,527	Art Unit: 1627
Cnfrm. No.	:	5780	
Filed	:	November 9, 2001	
For	:	DETECTION OF NUCLEIC ACID SEQUENCE DIFFERENCES USING THE LIGASE DETECTION REACTION WITH ADDRESSABLE ARRAYS	

REQUEST FOR DECLARATION OF INTERFERENCE UNDER 37 CFR §1.607(a)

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 CFR § 1.607(a), applicants hereby request that an interference be declared between the above-identified application and U.S. Patent No. 6,156,501 to McGall et al. ("'501 patent"). Both the '501 patent and the claims of the present application relate to oligonucleotide analogue arrays, a method of using the oligonucleotide analogue arrays to analyze interactions between an oligonucleotide target and an oligonucleotide probe, and a method of making the oligonucleotide analogue arrays. In addition, both the '501 patent and the claims of the present application relate to oligonucleotide arrays and a method of using the oligonucleotide arrays to detect oligonucleotide analogue targets. As demonstrated *infra*, a claim which is the same as, or for the same or substantially the same subject matter as, a claim of the '501 patent has been made in the above-identified application prior to one year from the date on which the '501 patent was granted. An interference should, therefore, be instituted between applicants' above-identified application and the '501 patent.

I. Information In Support Of Declaring An Interference.

37 CFR § 1.607(a) provides:

(a) An applicant may seek to have an interference declared between an application and an unexpired patent by,

(1) Identifying the patent,

(2) Presenting a proposed count,

(3) Identifying at least one claim in the patent corresponding to the proposed count,

(4) Presenting at least one claim corresponding to the proposed count or identifying at least one claim already pending in its application that corresponds to the proposed count, and, if any claim of the patent or application identified as corresponding to the proposed count does not correspond exactly to the proposed count, explaining why each such claim corresponds to the proposed count, and

(5) Applying the terms of any application claim,

(i) Identified as corresponding to the count, and

(ii) Not previously in the application to the disclosure of the application.

37 CFR § 1.607(a) (2001)

A. Identification of Patent

It is requested that the present application be put into interference with the '501 patent in which Glenn Hugh McGall, Charles Garrett Miyada, Maureen T. Cronin, Jennifer Dee Tan, and Mark S. Chee are named inventors and Affymetrix, Inc. is the assignee. The application corresponding to the '501 patent (i.e., U.S. Patent Application Serial No. 08/630,427 ("'427 application")) was filed on April 3, 1996, and the '501 patent was issued on December 5, 2000. The '427 application is a continuation-in-part of U.S. Patent Application Serial No. 08/440,742 ("'742 Application"), filed May 10, 1995, which is a continuation-in-part of PCT Application No. PCT/US94/12305, relating to oligonucleotide analogue arrays and methods of use. The PCT application was filed on October 26, 1994, and is a continuation-in-part of U.S. Patent Application Serial No. 08/284,064, filed August 2, 1994, now abandoned, which, in turn, is a continuation-in-part of U.S. Patent

Application Serial No. 08/143,312, filed October 26, 1993, now abandoned. As discussed *infra*, the claims of the '501 patent are only entitled to the May 10, 1995, filing date of the '742 application.

The present application, filed on November 9, 2001, is a continuation-in-part of U.S. Patent Application Serial No. 08/794,851 ("parent application"), filed February 4, 1997, currently pending, which claims the benefit of U.S. Provisional Patent Application Serial No. 60/011,359, filed February 9, 1996 ("grandparent application"). The present continuation-in-part application uses virtually the same disclosure as that of the parent application and the grandparent application, both of which support all pending claims, pursuant to 35 U.S.C. § 112 (first paragraph), as demonstrated in the attached Showing By Applicant Under 37 CFR § 1.608(b). The present application identifies Francis Barany, George Barany, and Robert P. Hammer as inventors. Cornell Research Foundation, Inc., Regents of the University of Minnesota, and Board of Supervisors of Louisiana State University and Agricultural and Mechanical College are the assignees of the present application, the parent application, and the aforementioned provisional application.

B. Proposed Count

Applicants propose the following count for purposes of initiating this interference:

Claim 1 of U.S. Patent Application Serial No. 09/986,527 ("'527 application")/Claim 1 of the '501 patent

or

Claim 12 of the '527 application/Claim 26 of the '501 patent

or

Claim 15 of the '527 application/Claim 35 of the '501 patent

or

Claim 25 of the '527 application/Claim 51 of the '501 patent

or

Claim 28 of the '527 application/Claim 58 of the '501 patent

or

Claim 33 of the '527 application

or

Claim 34 of the '527 application

or

Claim 35 of the '527 application

or

Claim 36 of the '527 application

or

Claim 37 of the '527 application

C. Claims of U.S. Patent No. 6,156,501 Corresponding to the Proposed Count

It is submitted that claims 1-72 of the '501 patent correspond to the proposed count.

D. Claims of the Present Application Corresponding to the Proposed Count

Claims 1-37 of the present application correspond to the proposed count.

E. Identification of Descriptive Support for the Claims Corresponding to the Proposed Count in the Original Disclosure of the Present Application

New claims 1-37 of the present application, which correspond to the proposed count and which differ from the claims of the parent application, are descriptively supported by the original disclosure of the present application as follows:

Claims of the Present Application	Descriptive Support in the Present Application
1. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 12, 33, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide analogue probes having different sequences,	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37). Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA,

Claims of the Present Application	Descriptive Support in the Present Application
	with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 12, 33, and 34).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations and	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 12, 33, and 34).
wherein said plurality of oligonucleotide analogue probes are selected to bind to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
2. The composition of claim 1, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
3. The composition of claim 1, wherein said solid substrate is selected from the group consisting of silica, polymeric materials, glass, beads, chips, and slides.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
4. The composition of claim 1, wherein said composition comprises an array of oligonucleotide analogue probes 4 to 20 nucleotides in length.	Discloses an array of oligonucleotides on a solid support with at least some of the array portions being occupied by oligonucleotides having greater

Claims of the Present Application	Descriptive Support in the Present Application
	than 16 nucleotides (page 7, lines 25-27). Discloses a 20 mer capture oligonucleotide (page 45, lines 17-18). Discloses assembling arrays with tetramers to produce capture oligonucleotides up to 24 nucleotides in length (page 38, line 20 to page 48, line 21).
5. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNAs), with either natural bases or nucleotide analogues (page 40, lines 35-37).
6. The composition of claim 1, wherein said solid substrate is attached to over 1000 different oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 8-10).
7. The composition of claim 1, wherein each probe of said plurality of oligonucleotide analogue probes has at least one oligonucleotide analogue, and wherein at least one of said oligonucleotide analogues comprises a nucleotide with a 5-propynyluracil base.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
8. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by light-directed chemical coupling.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23).
9. The composition of claim 8, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to page 27, line 2; page 50, line 17 to page 51, line 6).
10. The composition of claim 1, wherein said plurality of oligonucleotide analogue probes are coupled to said solid substrate by flowing oligonucleotide analogue reagents over known locations of the solid substrate.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
11. The composition of claim 10, wherein said solid substrate is derivitized with a silane reagent prior to synthesis of said plurality of oligonucleotide analogue probes.	Discloses silanizing the support surface with, e.g., 3-aminopropyl triethoxysilane (page 26, line 39 to page 27, line 2; page 50, line 17 to page 51, line 6).
12. A composition for analyzing the interaction between an oligonucleotide target and an oligonucleotide probe comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 33, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (see, e.g., claim 34). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific

Claims of the Present Application	Descriptive Support in the Present Application
	portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-36). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
wherein said oligonucleotide analogue targets bind to complementary oligonucleotide probes with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
13. The composition of claim 12, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses that oligonucleotides (normal and complementary directions, for capture hybridization) are prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 13, line 38 to page 14, line 2 and page 35, lines 1-10). Such analogues pair with perfect complementarity to the natural bases but increase T_m values (e.g., 5-propynyl-uracil) (page 40, lines 37-38).
14. The composition of claim 12, wherein at least one of said plurality of oligonucleotide probes comprise at least one oligonucleotide analogue.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
15. A method of analyzing interactions between an oligonucleotide target and an oligonucleotide probe comprising the steps of:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array of oligonucleotides on a solid support (see, e.g., claims 25, 35, and 36).
(a) synthesizing an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-15; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (see, e.g., claims 1, 12, 33,

Claims of the Present Application	Descriptive Support in the Present Application
	and 34).
wherein said oligonucleotide analogue probes are coupled to a solid substrate at known locations,	Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (see, e.g., claims 1, 12, 33, and 34).
said solid substrate having a surface;	Discloses a solid support having a substrate and a surface (page 25, lines 18-26).
(b) exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under hybridization conditions such that said plurality of oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
(c) determining whether an oligonucleotide analogue probe of said oligonucleotide probe array binds to at least one of said target nucleic acids.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
16. The method of claim 15, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
17. The method of claim 15, wherein said oligonucleotide target is genomic DNA.	Discloses the use of a DNA sample (page 12, lines 13-14 and 38-39).
18. The method of claim 15, wherein said target nucleic acid is amplified prior to said hybridization step.	Discloses that sample is amplified during the ligase detection reaction and prior to hybridization to oligonucleotide probes (page 15, lines 1-17; page 20, lines 5-12).
19. The method of claim 15, wherein said plurality	Discloses the use of positive/negative light reactive

Claims of the Present Application	Descriptive Support in the Present Application
of oligonucleotide analogue probes is synthesized on said solid support by light-directed synthesis.	protective groups (page 31, line 11 to page 32, line 23).
20. The method of claim 15, wherein said plurality of said oligonucleotide analogue probes is synthesized on said solid support by causing oligonucleotide analogue synthetic reagents to flow over known locations of said solid support.	Discloses application of solution including 5' amino-modified oligonucleotide to the solid support using a prefabricated mask (page 52, lines 3-22).
21. The method of claim 15, wherein said solid substrate is selected from the group consisting of beads, slides, and chips.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5). Discloses glass slides, chips, membranes, beads, and plastic supports as suitable solid supports (page 50, lines 9-13).
22. The method of claim 15, wherein said solid substrate is comprised of materials selected from the group consisting of silica, polymers and glass.	Discloses solid support including a substrate of functionalized glass, Si, Ge, GaAs, GaP, SiO_2, SiN_4, modified silicon, and polymers existing as particles, slides, etc., and a surface of polymers, plastics, ceramics, polysaccharides, silica or silica-based materials, carbon, metals, and inorganic glasses (page 25, lines 18-34; page 26, lines 1-5).
23. The method of claim 15, wherein the oligonucleotide analogue probes of said array are synthesized using photoremovable protecting groups.	Discloses the use of positive/negative light reactive protective groups (page 31, line 11 to page 32, line 23).
24. The method of claim 15, wherein at least one of said oligonucleotide analogue probes is synthesized from phosphoramidite reagents.	Discloses that phosphoramidite derivatives of 5-propynyl-dU can be prepared (page 35, lines 21-27).
25. A method of detecting an oligonucleotide target, comprising	Discloses an array of oligonucleotides on a solid support (claims 1, 12, 33, and 34)) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids (claims 15, 35, and 36).
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 29 to page 11, line 10). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 5-7).
selecting said oligonucleotide analogue targets such that said oligonucleotide analogue targets bind to	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific

Claims of the Present Application	Descriptive Support in the Present Application
the complementary oligonucleotide probes coupled to a solid surface at known locations of an array	portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
hybridizing the oligonucleotide analogue targets to complementary oligonucleotide probes; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
detecting whether at least one of said oligonucleotide analogue targets binds to said complementary oligonucleotide acid probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
26. The method of claim 25, wherein at least one of said oligonucleotide analogue targets has increased the thermal stability between said oligonucleotide analogue target and said complementary oligonucleotide probe as compared to an oligonucleotide target that is the perfect complement to the complementary oligonucleotide probe with which said oligonucleotide analogue target anneals.	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
27. The method of claim 25, wherein the oligonucleotide probe array comprises at least one oligonucleotide analogue probe which is complementary to at least one of said oligonucleotide analogue targets.	Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37) which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33). The ligated product sequence can be

Claims of the Present Application	Descriptive Support in the Present Application
	prepared with oligonucleotide probes which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
28. A method of making an array of oligonucleotide probes, comprising	Discloses a method for forming an array of oligonucleotides on a solid support (page 7, lines 13-14).
providing a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37).
said oligonucleotide analogue probes having different sequences at known locations on an array, and	Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1 and 33). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 1 and 33).
selecting the oligonucleotide analogue probes to hybridize with complementary oligonucleotide target sequences under hybridization conditions such that said oligonucleotide analogue probes bind to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
with a similar hybridization stability across the array.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
29. The method of claim 28, wherein at least one of said oligonucleotide analogue probes has increased the thermal stability between said oligonucleotide analogue probe and said	Discloses the use of 5-propynyl-dU in place of thymine to increase the thermal stability of DNA duplexes (page 35, lines 15-21; page 40, lines 8-13). Discloses that nucleotide analogues pair with

Claims of the Present Application	Descriptive Support in the Present Application
complementary oligonucleotide target as compared to an oligonucleotide probe that is the perfect complement to the complementary oligonucleotide target with which said oligonucleotide analogue probe anneals.	perfect complementarity to the natural bases but with increased T_m values (page 40, lines 37-38).
30. The method of claim 28 further comprising: incorporating a 5-propynyluracil base into the oligonucleotide analogue probes of the array.	Discloses the preparation of a PNA monomer having a 5-propynyl-uracil base component which can be incorporated into synthetic DNA and PNA strands to be linked to a solid support (page 36, lines 8-16).
31. The method of claim 28 further comprising: selecting said at least one oligonucleotide analogue such that oligonucleotide analogue probes comprises at least one peptide nucleic acid.	Discloses capture oligonucleotides prepared as either DNA or peptide nucleotide analogues (PNA), with either natural bases or nucleotide analogues (page 40, lines 35-37).
32. The method of claim 28 further comprising: providing said plurality of oligonucleotide analogue probes in an array with at least 1000 other oligonucleotide analogue probes.	Discloses that 1,000 different addresses can be unique capture oligonucleotide sequences linked covalently to the target-specific sequence of a LDR probe (page 24, lines 8-10).
33. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
a solid substrate and an array of a plurality of oligonucleotide analogue probes coupled to the solid substrate,	Discloses DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers attached to a solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 1, 12, and 34).
wherein the oligonucleotide analogue probes have different sequences and	Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1, 12, and 34).
are selected to hybridize to complementary oligonucleotide targets	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture

Claims of the Present Application	Descriptive Support in the Present Application
	oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
34. A composition for analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, and 33) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to the oligonucleotides on the array (claims 15, 25, 35, and 36).
an array of a plurality of oligonucleotide probes having different sequences	Discloses an array of oligonucleotides on a solid support (see, e.g., claim 12). Discloses a plurality of different capture oligonucleotides attached at different locations on a solid support (page 11, lines 35-37).
hybridized to complementary oligonucleotide analogue targets,	Discloses capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequences of oligonucleotide probes containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-36). The oligonucleotide probes can be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2).
wherein the oligonucleotide analogue targets hybridize to complementary oligonucleotide probes under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
35. A method of analyzing interactions between oligonucleotide targets and oligonucleotide probes comprising:	Discloses a method for detecting nucleic acid sequence differences in target nucleic acids by hybridization of nucleic acid sequences to an array

Claims of the Present Application	Descriptive Support in the Present Application
	of oligonucleotides on a solid support (see, e.g., claims 15, 25, and 36).
providing on a solid substrate an oligonucleotide analogue array comprising a plurality of oligonucleotide analogue probes having different sequences;	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 12-15; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (see, e.g., claims 1, 12, 33, and 34). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (see, e.g., claims 1, 12, 33, and 34).
exposing said oligonucleotide analogue probe array to a plurality of oligonucleotide targets under conditions effective to permit the plurality of oligonucleotide analogue probes to hybridize to complementary target oligonucleotides	Discloses contacting a ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions; and	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A•T content (page 35, lines 12-15).
determining whether an oligonucleotide analogue probe of said oligonucleotide probe array hybridizes to at least one of the oligonucleotide targets.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
36. A method of detecting an oligonucleotide target comprising:	Discloses an array of oligonucleotides on a solid support (claims 1, 12, 33, and 34) and its use in a method for detecting nucleic acid sequence differences in target nucleic acids (claims 15, 25,

Claims of the Present Application	Descriptive Support in the Present Application
	and 36).
enzymatically copying an oligonucleotide target using at least one nucleotide analogue, thereby producing multiple oligonucleotide analogue targets;	Disclose subjecting a sample potentially containing one or more nucleotide sequences with a plurality of sequence differences to ligase detection reaction (ligation phase) (page 10, line 29 to page 11, line 10). Discloses the use of oligonucleotide probes during the ligation phase, which may be peptide nucleotide analogues, modified peptide nucleotide analogues, or nucleotide analogues (page 13, line 38 to page 14, line 2) to produce a ligated product sequence of oligonucleotide probes containing (a) an addressable array-specific portion, (b) target-specific portions connected together, and (c) a detectable reporter label (page 11, lines 5-7).
providing on a solid substrate an oligonucleotide array comprising a plurality of oligonucleotide probes selected to hybridize to complementary oligonucleotide analogue targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions;	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).
exposing the oligonucleotide analogue targets to the oligonucleotide array under conditions effective to permit the oligonucleotide probes to hybridize to complementary oligonucleotide analogue targets; and	Discloses contacting ligated reaction product with a solid support including capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label. The addressable array-specific portion hybridizes to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
detecting whether at least one of the oligonucleotide analogue targets hybridizes to a complementary oligonucleotide probe.	Discloses detecting labels of oligonucleotide probes hybridized to the solid support (page 1, lines 20-22).
37. A method of making an array of	Discloses a method for forming an array of

Claims of the Present Application	Descriptive Support in the Present Application
oligonucleotide probes comprising:	oligonucleotides on a solid support (page 7, lines 13-14).
providing, on an array, a plurality of oligonucleotide analogue probes having at least one oligonucleotide analogue and different sequences,	Discloses attaching a plurality of different capture oligonucleotides at different locations on a solid support (page 11, lines 35-37). Discloses attaching DNA oligonucleotides or peptide nucleotide analogue (PNA) oligomers to the solid support (i.e., capture oligonucleotides include DNA oligonucleotides or PNA oligomers) (page 8, lines 10-13; page 30, lines 32-34). Discloses capture oligonucleotides prepared as either DNA or PNA, with either natural bases or nucleotide analogues (page 40, lines 35-37). Discloses a plurality of capture oligonucleotides each having different nucleotide sequences (claims 1 and 33). Discloses capture oligonucleotides immobilized at particular sites on a solid support (page 6, lines 37-38). Discloses a solid support including an array of positions with oligonucleotides attached to the array of positions (claims 1 and 33).
wherein the oligonucleotide analogue probes are selected to hybridize to complementary oligonucleotide targets	Discloses the use of capture oligonucleotides which are complementary to addressable array-specific portions of a ligated product sequence containing (a) the addressable array-specific portion, (b) target-specific portions connected together, and (c) the detectable reporter label, where the addressable array-specific portions are hybridized to the capture oligonucleotides in a base-specific manner (page 6, lines 28-33).
under uniform hybridization conditions.	Discloses method for high specificity detection of correct signal, independent of the target sequence, and under uniform hybridization conditions (page 49, lines 16-18). Discloses that oligonucleotide capture can be optimized by narrowing the thermal stability (T_m) difference between duplexes formed by capture oligonucleotides and the complementary addressable array-specific portions hybridized to one another resulting from differences in G•C/A T content (page 35, lines 12-15).

II. Conclusion

Having met all the requirements of the 37 CFR § 1.607(a), applicants hereby submit that an interference between the present application and the '501 patent should be declared.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date below.	
Jan. 7, 2002 Date	Ruth R. Smith Ruth R. Smith